

## **REMARKS**

### **I. Background**

The present amendment and remarks are in response to the Office Action mailed March 30, 2007. Claims 13-23 were pending in the application at the time of the Office Action. Applicant has amended claims 13 and 22, and added new claims 24-32. As such, claims 13-32 are currently pending for consideration on the merits.

Reconsideration of the claims is respectfully requested in view of the above amendments to the claims and the following remarks. For the Examiner's convenience and reference, Applicant's remarks are presented in the order in which the corresponding issues were raised in the Office Action.

Please note that the following remarks are not intended to be an exhaustive enumeration of the distinctions between any cited reference and the claimed invention. Rather, the distinctions identified and discussed below are presented solely by way of example to illustrate some of the differences between the claimed invention and the cited references. In addition, Applicant requests that the Examiner carefully review any reference discussed below to ensure that Applicant's understanding and discussion of the references, if any, is consistent with the Examiner's understanding.

### **II. Proposed Claim Amendments**

The amendments and new claims are fully supported by the specification and claims as originally filed. More particularly, new claims 24-32 are fully supported by the specification at paragraphs [0036-0052] (PG-Pub 2005/0233445). Thus, Applicant respectfully submits that the amendments to the claims do not introduce new matter and entry thereof is respectfully requested.

### **III. Rejection on the Merits**

The Office Action rejects claims 13-23 under 35 USC § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter. More

particularly, the Office Action asserts that there is no antecedent basis for “the components,” and that “like medium” is indefinite. In response, Applicant has amended independent claim 13, from which claims 14-23 depend, to provide antecedent basis for “components” and to clarify the “medium.” Thus, Applicant respectfully requests withdrawal of the rejection under 35 USC § 112, second paragraph.

The Office Action rejects claims 13, 15, 17-19, and 21-23 under 35 USC § 102(b) as being anticipated by the article by *Zhang et al* (In vitro Cell. Dev. Biol.-Animal 2001). Applicant respectfully traverses the rejection because the Office Action has not established that *Zhang* teaches each and every claim element in the presently pending claims.

Applicant respectfully asserts that the Office Action has mischaracterized the teachings of *Zhang*, and improperly combined the results of two separate and distinct experiments. *Zhang* does not teach that passing and dispersing rat urothelial cells (RUC) from a RUC culture, other than a primary RUC culture, leads to a differentiated multilayer structure. In fact, *Zhang* is completely devoid of teaching that RUCs that are cultured in media containing serum can be dispersed into another medium containing serum or undergo multiple passages in order to obtain the differentiated multilayer structure. In part, this is because *Zhang* does not teach that RUCs that are maintained up to passage 18 in medias containing serum can form the differentiated multilayer structure. On the other hand, *Zhang* only teaches that urothelial stratification could be induced by culturing RUCs either on irradiated 3T3 cells or in CM-KSFM (e.g., KSFM conditioned with 3T3 cell supernatant) for an extended duration before being detached as a stratified urothelial sheet, and nothing within *Zhang* indicates the RUCs underwent additional passages before producing the stratified urothelial sheet.

Accordingly, Applicant respectfully asserts that *Zhang* does not teach each and every element of the presently claimed invention recited in claim 13. More particularly, *Zhang* is completely devoid of teaching a “method of production of stratified, differentiated mammalian urothelium in which urothelial cells, isolated from the mammalian body, are passaged through a first nutrient medium containing components of serum and then redispersed before being added to a second medium containing components of serum to form said urothelium,” as recited in claim 13. In part, this is because *Zhang* is completely devoid of any teaching that

urothelium cells can be passaged through a first media containing serum before being redispersed and being cultured into a second media containing serum in order to form urothelium. Thus, *Zhang* does not teach each and every element of the presently claimed invention recited in claim 13.

Since *Zhang* does not teach each and every claim element, *Zhang* does not anticipate the presently claimed invention recited in claim 13. Since claims 15, 17-19, and 21-23 depend from claim 13, such claims include the same claim elements and are allowable for at least the same reasons that claim 13 is allowable. Thus, Applicant respectfully requests withdrawal of the rejection under 35 U.S.C. § 102(e) with respect to *Zhang*.

The Office Action rejects claims 13-15, 17, 18, 21, and 23 under 35 USC § 102(b) as being anticipated by the article by *Liebert et al.* (Differentiation 1997). Applicant respectfully traverses the rejection because the Office Action has not established that *Liebert* teaches each and every claim element in the presently pending claims.

Applicant respectfully asserts that *Liebert* does not teach each and every element of the presently claimed invention recited in claim 13. More particularly, *Liebert is completely devoid of teaching* a “method of production of stratified, differentiated mammalian urothelium in which urothelial cells, isolated from the mammalian body, are passaged through a first nutrient medium containing components of serum and then redispersed before being added to a second medium containing components of serum to form said urothelium,” as recited in claim 13. In part, this is because *Liebert* is completely devoid of any teaching that urothelium cells can be passaged through a first media containing serum before being redispersed and being added into a second media containing serum in order to form urothelium. In fact, once the urothelium cells of *Liebert* are cultured in a media containing serum, such cells are not dispersed into a second media containing serum before differentiation or stratification. Thus, *Liebert* does not teach each and every element of the presently claimed invention recited in claim 13.

Since *Liebert* does not teach each and every claim element, *Liebert* does not anticipate the presently claimed invention recited in claim 13. Since claims 14-15, 17, 18, 21, and 23 depend from claim 13, such claims include the same claim elements and are allowable for the same reasons that claim 13 is allowable. Thus, Applicant respectfully requests withdrawal of the

rejection under 35 U.S.C. § 102(e) with respect to *Liebert*.

The Office Action rejects claims 13-15, 17, 18, and 23 under 35 USC § 102(b) as being anticipated by the article by *Scriven et al.* (The Journal of Urology 1997). Applicant respectfully traverses the rejection because the Office Action has not established that *Scriven* teaches each and every claim element in the presently pending claims.

Applicant respectfully asserts that *Scriven* does not teach each and every element of the presently claimed invention recited in claim 13. More particularly, *Scriven is completely devoid of teaching* a “method of production of stratified, differentiated mammalian urothelium in which urothelial cells, isolated from the mammalian body, are passed through a first nutrient medium containing components of serum and then redispersed before being added to a second medium containing components of serum to form said urothelium,” as recited in claim 13. In part, this is because *Scriven* is completely devoid of any teaching that urothelium cells can be passed through a first media containing serum before being redispersed and being added into a second media containing serum in order to form urothelium. In fact, once the urothelium cells of *Scriven* are cultured in a media containing serum, such cells are not dispersed into a second media containing serum before differentiation or stratification. Thus, *Scriven* does not teach each and every element of the presently claimed invention recited in claim 13.

Since *Scriven* does not teach each and every claim element, *Scriven* does not anticipate the presently claimed invention recited in claim 13. Since claims 14-15, 17, 18, and 23 depend from claim 13, such claims include the same claim elements and are allowable for at least the same reasons that claim 13 is allowable. Thus, Applicant respectfully requests withdrawal of the rejection under 35 U.S.C. § 102(e) with respect to *Scriven*.

The Office Action rejects claim 16 under 35 USC § 103(a) as being obvious over the articles by *Zhang*, *Liebert*, or *Scriven* in view of *Seijiro et al.* (U.S. Patent No. 4,654,304). Applicant respectfully asserts that the Office Action has not established a *prima facie* case of obviousness because the proposed combination of references (e.g., *Zhang*, *Liebert*, or *Scriven* in combination with *Seijiro*) does not teach or suggest each and every element of the presently claimed invention.

The foregoing discussions of *Zhang*, *Liebert*, and/or *Scriven* are applicable to this rejection, and are hereby incorporated into this remark by specific reference. Applicant respectfully asserts that *Sejiro* does not cure the deficiencies of *Zhang*, *Liebert*, and/or *Scriven*, which were discussed above. In part, this is because **Sejiro is completely devoid of teaching or suggesting** a “method of production of stratified, differentiated mammalian urothelium in which urothelial cells, isolated from the mammalian body, are **passed through a first nutrient medium containing components of serum** and **then redispersed** before **being added to a second medium containing components of serum** to form said urothelium,” as recited in claim 13. Thus, the combination of references (e.g., *Zhang*, *Liebert*, or *Scriven* in combination with *Sejiro*) does not teach or suggest each and every element of the presently claimed invention as recited in claim 13.

Since the combination of references (e.g., *Zhang*, *Liebert*, or *Scriven* in combination with *Sejiro*) does not teach or suggest each and every element of the presently claimed invention, a *prima facie* case of obviousness has not been established with respect to claim 13. Since claim 16 depends from claim 13, claim 16 includes the same claim elements and is allowable for at least the same reasons claim 13 is allowable. Thus, Applicant respectfully requests withdrawal of the rejection of claim 16 under 35 U.S.C. § 103(a).

The Office Action rejects claim 20 under 35 USC § 103(a) as being obvious over *Zhang* in view of *Judd et al.* (U.S. Patent No. 6,692,961). Applicant respectfully asserts that the Office Action has not established a *prima facie* case of obviousness because the proposed combination of *Zhang* and *Judd* does not teach or suggest each and every element of the presently claimed invention.

The foregoing discussion of *Zhang* is applicable to this rejection, and is hereby incorporated into this remark by specific reference. Applicant respectfully asserts that *Judd* does not cure the deficiencies of *Zhang*. In part, this is because **Judd is completely devoid of teaching or suggesting** a “method of production of stratified, differentiated mammalian urothelium in which urothelial cells, isolated from the mammalian body, are **passed through a first nutrient medium containing components of serum** and **then redispersed** before **being added to a second medium containing components of serum** to form said urothelium,” as

recited in claim 13. Thus, the combination of *Zhang* and *Judd* does not teach or suggest each and every element of the presently claimed invention as recited in claim 13.

Since the combination of *Zhang* and *Judd* does not teach or suggest each and every element of the presently claimed invention, a *prima facie* case of obviousness has not been established with regard to claim 13. Since claim 20 depends from claim 13, claim 20 includes the same claim elements and is allowable for at least the same reasons claim 13 is allowable. Thus, Applicant respectfully requests withdrawal of the rejection of claim 20 under 35 U.S.C. § 103(a).

The Office Action rejects claims 20 and 22 under 35 USC § 103(a) as being obvious over *Liebert* article in view of *Judd*. Applicant respectfully asserts that the Office Action has not established a *prima facie* case of obviousness because the proposed combination of *Liebert* and *Judd* does not teach or suggest each and every element of the presently claimed invention.

The foregoing discussion of *Liebert* is applicable to this rejection, and is hereby incorporated into this remark by specific reference. Applicant respectfully asserts that *Judd* does not cure the deficiencies of *Liebert*. In part, this is because *Judd* is completely devoid of teaching or suggesting a “method of production of stratified, differentiated mammalian urothelium in which urothelial cells, isolated from the mammalian body, are passaged through a first nutrient medium containing components of serum and then redispersed before being added to a second medium containing components of serum to form said urothelium,” as recited in claim 13. Thus, the combination of *Liebert* and *Judd* does not teach or suggest each and every element of the presently claimed invention as recited in claim 13.

Since the combination of *Liebert* and *Judd* does not teach or suggest each and every element of the presently claimed invention, a *prima facie* case of obviousness has not been established with regard to claim 13. Since claims 20 and 22 depend from claim 13, claims 20 and 22 each include the same claim elements and is allowable for the same reasons claim 13 is allowable. Thus, Applicant respectfully requests withdrawal of the rejection of claims 20 and 22 under 35 U.S.C. § 103(a).

#### **IV. New Claims**

Applicant respectfully asserts that new claims 24-32 are allowable for at least the same reasons claim 13 is allowable. None of the references recited in the rejections to the claims teaches or suggests a method having the following steps: "dispersing the urothelial cells of the primary culture into a second cell culture medium that includes serum; culturing the urothelial cells in the second culture medium to form a secondary cell culture having aggregated urothelial cells; dispersing the aggregated urothelial cells into a third cell culture medium that includes serum; and culturing the urothelial cells in the third culture medium to form stratified, differentiated mammalian urothelium," as recited in claim 24. Additionally, the references recited in the rejections do not provide any motivation, suggestion, or reason for one of ordinary skill in the art to perform such a method. Furthermore, dispersal of cells grown in a media containing serum constitutes an action that is apparently diametrically opposed to achieving the desired result of an differentiated, stratified urothelium. As such, the skilled artisan would seek to maintain any structure from the first culture stage rather than disrupting it, and would have no motivation, suggestion, or reason to disrupt the cell culture of urothelial cells grown in media containing serum and then disperse the urothelial cells into another media containing serum. Thus, Applicant submits that new claims 24-32 are allowable over the references recited in the rejections discussed herein.

#### **Conclusion**

In view of the foregoing, Applicant respectfully submits that the other rejections to the claims are now moot and do not, therefore, need to be addressed individually at this time. It will be appreciated, however, that this should not be construed as Applicant acquiescing to any of the purported teachings or assertions made regarding the cited art or the pending application, including any Official Notice. Instead, Applicant reserves the right to challenge any of the purported teachings or assertions made in any action at any appropriate time in the future, should the need arise. Furthermore, to the extent that the Examiner has relied on any Official Notice, explicitly or implicitly, Applicant specifically requests that the Examiner provide references supporting the teachings officially noticed, as well as the required motivation or suggestion to combine the relied upon Notice with the other art of record.

Applicant believes claims 13-32 are in allowable form as discussed above. As such, Applicant respectfully requests reconsideration of the application and allowance of presently pending claims.

In the event that the Examiner finds remaining impediment to a prompt allowance of this application that may be clarified through a telephone interview, the Examiner is requested to contact the undersigned attorney by telephone at (801) 533-9800.

Dated this 28<sup>th</sup> day of June 2007.

Respectfully submitted,

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